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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,759	03/03/2006	Mingdong Zhou	11748-006-999	7322

20583 7590 12/08/2009

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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
12/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,759	ZHOU, MINGDONG	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6,9-14,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6,9-14,44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 11, 2009 has been entered.

Claims 4, 6, 9-14, 44, and 45 are currently pending and being examined. Claims 4, 9, 10 are amended.

NEW REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 4, 6, 9-14, 44, and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are now drawn to a method for preventing, treating or delaying neoplasm in a mammal, which method comprises administering to a mammal, to which such prevention, treatment or delay is needed or desirable, an effective amount of an ErbB-3 protein, whereby an immune response is generated against said neoplasm is prevented, treated or delayed, **wherein the ErbB-3 protein comprises: (b) amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 protein is not the extracellular domain of ErbB-3.**

The specification discloses that any suitable ErbB-3 protein or functional fragment thereof that can elicit an immune response to the neoplasm can be used in the present method. The specification discloses that ErbB-3 proteins or fragments disclosed in US Patent 5,820,859 can be used, or those derived from rat ErbB-3, from puffer fish ErbB-3, or derived from human ErbB-3 (p. 12, section B). The specification discloses that the invention encompasses proteins which comprise an extracellular domain of the ErbB-3 protein which comprise an amino acid sequence set forth in SEQ ID NO:2 or SEQ ID NO:3 (p. 4 and 13). SEQ ID NO:2 is 640 amino acids long and SEQ ID NO:3 is 190 amino acids long. The specification discloses that an extracellular domain of an ErbB-3 protein may be administered in the invention (p. 13, first full paragraph). The specification discloses in section C, pages 17-18 that there are plural "extracellular domains of ErbB-3 protein" and these can comprise SEQ ID NO:2 or 3, an amino acid sequence comprising at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, or an amino acid sequence comprising at least amino acid residues 2-139 of the amino acid sequence set forth in SEQ ID NO:16 (p. 17 bridging to

p. 18). The specification discloses pharmaceutical compositions comprising an extracellular domain of ErbB-3 protein comprising an amino acid sequence set forth in SEQ ID NO:2 or 3 or at least amino acid residues 24-81 of SEQ ID NO:14 or at least amino acid residues 2-139 of SEQ ID NO:16 (p. 21, last paragraph). The specification repeatedly discloses proteins or nucleic acids encoding "an extracellular domain of the ErbB-3 protein" and discloses plural forms of extracellular domains, indicating there is more than one extracellular domain in the invention. The specification discloses that SEQ ID NO:14, also named rhErbB3-f12, was used to inoculate mice. It appears rhErbB3-f12 reduced tumor growth in inoculated mice compared to controls, however the type of cancer the mice developed is unclear (i.e., breast, lung, etc) (Table 4, p. 30). There are no examples disclosing administration of a protein consisting of amino acid residues 24-81 of SEQ ID NO:14. The specification does not disclose any ErbB-3 protein comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 protein is not the extracellular domain of ErbB-3 and functions to generate an immune response and prevent, treat, or delay a neoplasm as broadly encompassed in the claims.

The art teaches various extracellular domains of ErbB-3. For example, Lee et al (Cancer Research, 2001, 61:4467-4473, IDS) teach the extracellular domain is the amino terminal residues 1-620 (Figure 1). Kraus et al (PNAS 1989, 9193-9197, IDS) teach the extracellular domain of ErbB-3 is amino acids 20-643 of Figure 3. These various domains do not provide an adequate representative number of species to support adequate written description for the broad genus of extracellular domains of

ErbB-3 or ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB-3 that function to generate an immune response and prevent, treat, or delay a neoplasm as encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "the ErbB-3 protein comprises: (b) amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 protein is not the extracellular domain of ErbB-3". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure,

formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an

invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of extracellular domains of ErbB-3 or ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB-3 that function to generate an immune response and prevent, treat, or delay a neoplasm, per Lilly by structurally describing representative ErbB-3 proteins or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe extracellular domains of ErbB-3 or ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB-3 that function to generate an immune response and prevent, treat, or delay a neoplasm useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses plural "extracellular domains of ErbB-3 protein" that can comprise various sequences set forth above and exemplifies protein SEQ ID NO:14 functioning to treat a tumor, this does not provide a description of the broadly claimed extracellular domains of ErbB-3 or ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB-3 that function to generate an immune response and prevent, treat, or delay a neoplasm that would satisfy the standard set out in Enzo because the specification provides no structural features coupled to the functional characteristics of generating an immune response against the neoplasm and preventing, treating, or delaying the neoplasm.

Further, the specification also fails to describe extracellular domains of ErbB-3 or ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB-3 that function to generate an immune response and prevent, treat, or delay a neoplasm by the test set out in Lilly because the specification describes plural "extracellular domains of ErbB-3 protein" that can comprise various sequences as set forth above. Therefore it necessarily fails to describe a representative number of such

species. In other words, the specification and claims do not identify which structural features are conserved among the extracellular domains of ErbB-3 or the ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB-3 that function to generate an immune response and prevent, treat, or delay a neoplasm, or which structures constitute a substantial portion of the genus in order for one to visualize or recognize the identity of the members of the genus. While the claims exclude "the extracellular domain of ErbB-3" from being used in the claimed method, it is entirely unclear from the specification what constitutes "the" extracellular domain of ErbB-3 given the plural and various domains disclosed in the specification and the art (Lee et al and Kraus et al above) and given ErbB-3 can be derived from any species.

Thus, the specification does not provide an adequate written description of extracellular domains of ErbB-3 or ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB-3 that function to generate an immune response and prevent, treat, or delay a neoplasm that is required to practice the claimed invention. Since the specification fails to adequately describe the product to which the claimed method uses, it also fails to adequately describe the method.

Rejection Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. **Claims 4, 6, and 9-14, 44, and 45 remain rejected under 35 U.S.C. 102(b)** as being anticipated by WO 98/02540, Fizpatrick et al, published 1/22/1998 (see section 4 of the previous Office Action).

The claims are now drawn to a method for preventing, treating or delaying neoplasm in a mammal, which method comprises administering to a mammal, to which such prevention, treatment or delay is needed or desirable, an effective amount of an ErbB-3 protein, whereby an immune response is generated against said neoplasm is prevented, treated or delayed, wherein the ErbB-3 protein comprises: (b) amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 protein is not the extracellular domain of ErbB-3 (claim 4), the method of claim 4, further comprising administering an immune response potentiator to the mammal (claim 6), the method of claim 4, wherein the ErbB-3 protein is co-administered with a pharmaceutically acceptable carrier or excipient (claim 9), the method of claim 4, wherein the ErbB-3 protein is co-administered with an anti-neoplasm agent (claim 10), the method of claim 10, wherein the anti-neoplasm agent is selected from the group consisting of an anti-angiogenic agent, an alkylating agent, an antimetabolite, a natural

product, a platinum coordination complex, an anthracenedione, a substituted urea, a methylhydrazine derivative, an adrenocortical suppressant, a hormone, an antagonist, an oncogene inhibitor, a tumor suppressor gene or protein, an anti-oncogene antibody and an anti-oncogene antisense oligonucleotide (claim 11), the method of claim 4, wherein the neoplasm to be prevented, treated or delayed is breast cancer (claims 12-14), the method of claim 4, wherein the mammal is a human (claim 44), the method of claim 4, wherein the administering is by intracavernous injection, subcutaneous injection, intravenous injection, intramuscular injection, intradermal injection, oral administration or topical administration (claim 45).

It is noted that the instant specification provides a broad definition of extracellular domains of ErbB-3, which can comprise SEQ ID NO:2 or 3, an amino acid sequence comprising at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, or an amino acid sequence comprising at least amino acid residues 2-139 of the amino acid sequence set forth in SEQ ID NO:16, and ErbB-3 can be derived from any species, as stated in the rejection above.

Fizpatrick et al teach a method for treating or preventing a neoplasm in a mammal comprising administering to the mammal an ErbB-3 protein comprising an extracellular domain protein of human ErbB-3 (p. 8, line 38 through p. 9, line 12; p. 9, lines 32 through p. 10, line 3; p. 19, lines 31-33; p. 27, lines 8-9; Examples 2-3; claims 7, 37, 38), wherein the neoplasm is breast cancer (p. 15, line 10; p. 25, lines 1-10), wherein the mammal is human (p. 19, lines 34-36), wherein the ErbB-3 protein is administered in a pharmaceutically acceptable carrier or excipient (p. 19, lines 37 to p.

20, line 2; p. 26, lines 3-14), wherein the ErbB-3 protein is administered with an immune response potentiator or adjuvant such as a cytokine (p. 27, lines 19-20), wherein the ErbB-3 protein is co-administered with an antineoplastic agent which includes anti-angiogenic agents and antibody antagonists of oncogene growth receptors (p. 27, 10-20), wherein the ErbB-3 protein is administered by intravenous, intraperitoneal, intraarterial injection (p. 26, lines 22-25), and wherein the ErbB-3 protein comprises the N-terminal 636 amino acids (p. 35, line 25), which necessarily comprises at least amino acid residues 24-81 of SEQ ID NO:14 of the instant application (residues 24-81 are the equivalent of residues 483-540 of ErbB-3). Given Fizpatrick et al teach a method for treating or preventing a neoplasm in a mammal comprising the same claimed step of administering to the mammal the extracellular domain protein of human ErbB-3, the method taught by Fizpatrick et al would generate an immune response against said neoplasm. Given the ErbB-3 protein comprises the N-terminal 636 amino acids, it would not be "the extracellular domain of ErbB-3" according to the instant specification when the extracellular domain is defined as SEQ ID NO:2 or 3 or when the extracellular domain is of a species other than human.

Response to Arguments

4. Applicants argue that Fizpatrick et al does not teach or suggest any of the recited ErbB-3 protein. Applicants argue that Fizpatrick et al discloses soluble cimeric heteromultimers containing the extracellular domain of ErbB-3. Applicants argue that

claim was amended to recite that the ErbB-3 protein is not the extracellular domain of ErbB-3 (p. 5-6).

The arguments have been considered but are not found persuasive because Applicants are arguing limitations not recited in the claims. As stated in the rejection above, Fizpatrick et al teach using an ErbB-3 protein that comprises the N-terminal 636 amino acids (p. 35, line 25), which necessarily comprises at least amino acid residues 24-81 of SEQ ID NO:14 of the instant application (residues 24-81 are the equivalent of residues 483-540 of ErbB-3). Given the ErbB-3 protein comprises the N-terminal 636 amino acids, it would not be "the extracellular domain of ErbB-3" according to the instant specification when the extracellular domain is defined as SEQ ID NO:2 (640 amino acids) or SEQ ID NO:3 (190 amino acids) or when the extracellular domain is of a species other than human.

5. All other rejections recited in the Office Action mailed June 11, 2009 are hereby withdrawn.

6. **Conclusion:** No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642